

IN THE CLAIMS

Claim 1 (original): A vaccine composition lacking preventive or curative immunosuppressive property towards a cancer caused by a Papillomavirus infection, characterized in that it comprises, as the active ingredient, a non immunosuppressive mutated E7 protein, comprising the amino acid sequence consisting, from the N-terminal end to the C-terminal end, in:

- i. the 1-19 amino acid sequence of sequence SEQ ID No. 3;
- ii. an amino acid sequence possessing (a) the substitution of at least one amino acid, compared to the 20-29 corresponding amino acid sequence of sequence SEQ ID No. 3 or (b) the deletion of at least four consecutive amino acids, compared to the 20-29 corresponding amino acid sequence of sequence SEQ ID No. 3; and
- iii. the 30-98 amino acid sequence of sequence SEQ ID No. 3, in association with one or more physiologically compatible immunity adjuvants.

Claim 2 (original): A vaccine composition according to claim 1, wherein the mutated E7 protein is characterized in that the amino acid region (ii) of said mutated E7 protein comprises at least two substitutions of amino acids, compared to the corresponding 20-29 peptide region of amino acids of sequence SEQ ID No. 3 of the native protein.

Claim 3 (original): A vaccine composition according to claim 2, wherein the mutated E7 protein is characterized in that the amino acid region (ii) of said mutated E7 protein comprises three, four, five, six, seven, eight, nine or ten substitutions of amino acids, compared to the corresponding 20-29 peptide region of amino acids of sequence SEQ ID No. 3 of the native protein.

Claim 4 (original): A vaccine composition according to claim 2, wherein the mutated E7 protein is characterized in that the Cys residues in position 24 and Glu in position 26 have been substituted by a distinct amino acid residue.

Claim 5 (original): A vaccine composition according to claim 4, wherein the mutated E7 protein is the (CYS24GLY, GLU26GLN) E7 protein.

Claim 6 (original): A vaccine composition according to claim 4, wherein the mutated E7 protein is the (CYS24SER, GLU26GLN) E7 protein.

Claim 7 (original): A vaccine composition according to claim 1, wherein the mutated E7 protein is characterized in that the amino acid region (ii) of said mutated E7 protein comprises the deletion of five, six, seven, eight, nine or ten consecutive amino acids, compared to the corresponding 20-29 amino acid sequence of SEQ ID No. 3.

Claim 8 (original): A vaccine composition according to claim 7, wherein the mutated E7 protein is characterized in that the amino acid region (ii) of said mutated E7 protein comprises the deletion of six consecutive amino acids, compared to the corresponding 20-29 amino acid sequence of SEQ ID No. 3.

Claim 9 (original): A vaccine composition according to claim 8, wherein the mutated E7 protein consists in the mutated E7 protein having the amino acid sequence comprising the deletion of the corresponding amino acids 21 to 26 of the SEQ ID No. 3 sequence of the native E7 protein.

Claim 10 (original): A vaccine composition according to claim 7, wherein the mutated E7 protein is characterized in that the amino

acid region (ii) of said mutated E7 protein comprises the deletion of five consecutive amino acids, compared to the corresponding 20-29 amino acid sequence of SEQ ID No. 3.

Claim 11 (original): A vaccine composition according to claim 10, wherein the mutated E7 protein consists in the mutated E7 protein having the amino acid sequence comprising the deletion of the corresponding amino acids 21 to 25 of the SEQ ID No. 3 sequence of the native E7 protein.

Claim 12 (currently amended): A vaccine composition according to claim 1 ~~one of claims 1 to 11~~, characterized in that it comprises at least one adjuvant able to preferably orient the immune response towards the production of antibodies neutralizing the immunosuppressive activity of the native E7 protein.

Claim 13 (original): A vaccine composition according to claim 12, characterized in that it comprises at least one adjuvant able to preferably orient the immune response towards the production of IgA isotype antibodies.

Claim 14 (original): A vaccine composition according to claim 12, characterized in that it comprises at least one adjuvant able to preferably orient the immune response towards the production of IgG isotype antibodies.

Claim 15 (original): A vaccine composition according to claim 12, characterized in that it comprises the combination (i) of one adjuvant able to preferably orient the immune response towards the production of IgA isotype antibodies and (ii) of one adjuvant able to preferably orient the immune response towards the production of IgG isotype antibodies.

Claim 16 (original): A vaccine composition according to claim 15, characterized in that it comprises at least one immunity adjuvant able to induce a humoral and cellular immune response.

Claim 17 (original): A vaccine composition according to claim 7, characterized in that the cellular response is characterized more particularly by the proliferation of lymphocytes expressing the CD8 antigen and specifically recognizing the wild E7 protein.

Claim 18 (original): An immunogenic composition inducing an immune response towards the HPV-16 Papillomavirus native E7 protein, without simultaneously inducing an immunosuppression, said composition comprising, as the active ingredient, a non immunosuppressive mutated E7 protein, comprising the amino acid sequence consisting, from the N-terminal end to the C-terminal end, in:

- i. the 1-19 amino acid sequence of sequence SEQ ID No. 3;
- ii. an amino acid sequence possessing (a) the substitution of at least one amino acid, compared to the 20-29 corresponding amino acid sequence of sequence SEQ ID No. 3 or (b) the deletion of at least four consecutive amino acids, compared to the 20-29 corresponding amino acid sequence of sequence SEQ ID No. 3; and
- iii. the 30-98 amino acid sequence of sequence SEQ ID No. 3, in association with one or more physiologically compatible excipients or immunity adjuvants.

Claim 19 (currently amended): A preventive or curative vaccine composition for a cancer caused by a HPV-16 infection, characterized in that it comprises an immunologically efficient amount of a nucleic acid encoding a mutated E7 protein, such as defined in claim 1 ~~one of claims 1 to 11~~, an expression cassette comprising said nucleic acid or a recombinant vector comprising said expression cassette.

Claim 20 (currently amended): A use of a non immunosuppressive mutated E7 protein such as defined in claim 1 ~~any of claims 1 to 11~~, for preparing a non immunosuppressive immunogenic composition or a vaccine composition and which induces the production of an antibody neutralizing the immunosuppressive activity of the native E7 protein.

Claim 21 (currently amended): Neutralizing antibodies directed against the expression product of the DNA encoding the mutated E7 protein such as defined according to claim 1 ~~one of claims 1 to 11~~.

Claim 22 (original): A composition for passive vaccination towards a HPV-16 infection containing antibodies according to claim 21.

Claim 23 (currently amended): A vaccine composition lacking any preventive or curative immunosuppressive property towards a cancer caused by a Papillomavirus infection, characterized in that it comprises, as the active ingredient, an appropriate amount of autologous or allogenic dendritic cells towards the individual to be treated, said autologous dendritic cells having been incubated with a mutated E7 protein such as defined in claim 1 ~~one of claims 1 to 11~~ and thereby made able to present said mutated E7 protein to T cells.

Claim 24 (new): A method of preventing or treating some cancers associated with an infection through the HPV-16 type Papillovirus which comprises inoculating a subject prone to or afflicted with such a cancer with a vaccine composition according to claim 1.